

carried out on asymptomatic women, be limited to those 35 years of age and older.

The x-ray diagnosis of cancer is usually made because of a mass with or without calcification or because of calcification alone. In occult lesions, precise preoperative localization of the lesion as well as x-ray studies of the specimen are necessary in many cases. X-ray examination should never replace physical examination because, like nearly all medical tests, it is not totally accurate in the detection of cancer. When dominant mass lesions are noted on physical examination, biopsy studies should be done even if findings on a xeromammogram are negative. Nonetheless, xeromammography appears to be an excellent method of diagnosing carcinoma of the breast and, at present, offers the best opportunity for diagnosis of occult carcinoma.

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The Stilbestrol-Adenosis-Carcinoma Syndrome

ALERTED BY A sequence of seven adolescent girls with adenocarcinoma of the vagina seen in 1966 and thereafter, we conducted and reported in 1971 a review study with suitable controls showing an extraordinary association between the lesion and antenatal exposure to diethylstilbestrol (DES).

Rapid dissemination of this fact during the development of a worldwide registry of such cases soon brought to medical attention numbers of girls and young women known to have been similarly exposed. Findings on examination showed that in most there were anomalies of development of the vagina and cervix, including unusually broad cervical erosion (ectropion), cervicovaginal ridges or furrows and extensive patches of vaginal adenosis. Persons exposed before the eighth week of pregnancy are most likely to show teratogenic effects; initiation of DES therapy after 18 weeks have elapsed apparently no longer carries this risk.

In most of the patients with carcinoma there have been coexisting areas of benign adenosis, but transition from one to the other has not yet been shown. The preferred treatment for benign adenosis, therefore, is not yet clearly established. Although it is tempting to recommend mechanical excision or destruction, the extent and distribution of patches of abnormal epithelium detected by colposcopy, Schiller's testing, biopsy or cytology is often such that it would require a formidable procedure and some risk of permanent deformity or stenosis.

Carcinoma has developed in only a small fraction of the women at risk, perhaps in less than one per thousand. The tumors are usually adenocarcinomas of the clear-cell type and can be successfully treated either by surgical procedures or radiation. However, spread by lymphatics is early, and tumors more advanced than stage II (Federation Internationale de Gynecologie et d'Obstetrique [FIGO] classification for cervix or vagina) are likely to have extended to the pelvic nodes. Adequate treatment for cure cannot avoid sacrifice of fertility, but sexual function is well preserved in patients amenable to radical surgical resection with simultaneous replacement of the vagina by a skin graft over a mold.

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Immunology in Fertility

THE PROBLEM of infertility and immunology is multifaceted. Men with sperm agglutinins and oligospermia or azospermia, women with hostile cervical mucous, couples with unexplained infertility and women with early spontaneous abortions may all fall victim to an immune reaction.

It has been known for some time that men with vasectomies or with obstructive duct disease may develop sperm agglutinins and immobilizing antibodies. Findings in recent studies have shown that in a significant percentage of infertile couples, these same antibodies can be found in the sera of the husband and wife as well as in semen.

Tien, in a review article, emphasized the general principles concerning this problem:

- Antisperm antibodies can occur in certain patients.
- Ten to thirty percent of unexplained infertility could be due to antibodies.
- Immobilizing antibodies appear to have a better correlation with infertility than do agglutinating antibodies (though Shulman has other evidence on that point).
- Condom therapy deserves a trial.

However, inconsistencies and contradictions still abound. A recent study was carried out on patients in whom results on postcoital tests were poor, that is, dead or nonmotile sperm being found in otherwise normal cervical mucus. Sixty-four women were studied with the immunofluorescent technique. In 30 percent there was a positive titer. However, there was a positive titer in 26 of 50 women with a known cause for infertility and *normal* findings on postcoital tests. The complexity of the immune reaction is such that diverse reports are to be expected.

Basic and clinical research continues. A study is being carried out to investigate antibody forma-

tion within hostile cervical mucus. There are centers now investigating the use of "donor" cervical mucus and homologous insemination for those patients with hostile cervical mucus. Embryos and zygotes have been studied and found to elicit antibody response with destruction of the developing embryo or placenta. Antibodies have been found in uterine fluid which notably reduce survival of embryos in test animals.

When the pieces of the puzzle are finally put together we will not only have a treatment for some patients with unexplained infertility but also possibly the best contraceptive to date.

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